

Claims

We claim:

1. A multi-functional contrast agent comprising a CdS:Mn/ZnS core/shell quantum dot, wherein said quantum dot is fluorescent, radio-opaque, and paramagnetic.
2. The contrast agent of claim 1, wherein said contrast agent further comprises a targeting moiety conjugated to said quantum dot.
3. The contrast agent of claim 1 or 2, wherein said contrast agent further comprises a targeting moiety conjugated to said quantum dot, wherein said targeting moiety is selected from the group consisting of a polypeptide, nucleic acids, carbohydrate, lipid, hormone, growth factor, receptor ligand, antigen, and antibody.
4. The contrast agent of any of claims 1 to 3, wherein said contrast agent further comprises a targeting moiety conjugated to said quantum dot, wherein said targeting moiety comprises a TAT peptide or folic acid.
5. The contrast agent of any of claims 1 to 4, wherein said contrast agent further comprises a coating (outer shell) surrounding said ZnS shell.
6. The contrast agent of any of claims 1 to 5, wherein said contrast agent further comprises a coating (outer shell) and a targeting moiety conjugated to said coating.
7. The contrast agent of any of claims 1 to 6, wherein said ZnS shell of said contrast agent is amine functionalized.
8. The contrast agent of any of claims 1 to 7, wherein said contrast agent further comprises an amine functionalized silica coating around said ZnS shell.

9. The contrast agent of any of claims 1 to 8, wherein said quantum dot is water-dispersable.

10. The contrast agent of any of claims 1 to 9, wherein said CdS:Mn/ZnS core/shell quantum dot further comprises a Gd (III)/SiO₂ coating (outer shell) or a Dys/SiO₂ coating (outer shell).

11. The contrast agent of any of claims 1 to 10, wherein said quantum dot is doped with a fluorescent dye molecule or a paramagnetic material, or both.

12. The contrast agent of any of claims 1 to 10, wherein said quantum dot further comprises a coating that renders said contrast agent activatable in a cell.

13. The contrast agent of any of claims 1 to 10, wherein said quantum dot further comprises a coating that renders said contrast agent activatable in a cell, and wherein said coating is a carbohydrate.

14. The contrast agent of any of claims 1 to 10, wherein said quantum dot further comprises a coating that renders said contrast agent activatable in a cell, and wherein said coating is a carbohydrate selected from the group consisting of galactose, glycogen, or glucose.

15. The contrast agent of claim 10, wherein said quantum dot further comprises a Gd (III)/SiO₂ coating (outer shell), and wherein said quantum dot further comprises a carbohydrate that blocks the ninth coordination site of Gd in the absence of a carbohydrate-degrading enzyme.

16. The contrast agent of any of claims 1 to 15, wherein said quantum dot is in the range of 3.0 nm and 100 nm in diameter.

17. The contrast agent of any of claims 1 to 16, wherein said quantum dot has a coating (outer shell) 2.0 nm to 50 nm in thickness.

18. A method for visualizing a target within an opaque medium using a multi-functional contrast agent of any of claims 1 to 16, wherein said method comprising introducing the contrast agent into the target or into the opaque medium and visualizing the target.

19. The method of claim 18, wherein said opaque medium comprises living or dead biological tissue and said visualizing is carried out *in vitro* or *in vivo*.

20. The method of claim 18, wherein said target comprises a living or dead cell and said visualizing is carried out *in vitro* or *in vivo*.

21. The method of any of claims 18 to 20, wherein said target comprises a vascular cell or vascular tissue *in vitro* or *in vivo*.

22. The method of any of claims 18 to 21, wherein said target comprises a vascular endothelial cell or vascular endothelial tissue *in vitro* or *in vivo*.

23. The method of any of claims 18 to 20, wherein said target comprises a neural cell or neural tissue *in vitro* or *in vivo*.

24. The method of any of claims 18 to 20, wherein said target comprises a brain cell or brain tissue *in vitro* or *in vivo*.

25. The method of any of claims 18 to 20, wherein said target comprises a cancer cell or cancer tissue *in vitro* or *in vivo*.

26. The method of any of claims 18 to 20, wherein said target comprises a tumor cell or tumor tissue *in vitro* or *in vivo*.

27. The method of any of claims 18 to 26, wherein said target comprises a human cell or human tissue *in vitro* or *in vivo*.

28. The method of any of claims 18 to 27, wherein said contrast agent includes a targeting moiety.

29. The method of claim 28, wherein said targeting moiety comprises a TAT peptide or folic acid.

30. The method of any of claims 18 to 29, wherein said quantum dot further comprises Gd (III)/SiO₂ coating (outer shell) and a carbohydrate, wherein the carbohydrate blocks the ninth coordination site of Gd in the absence of a carbohydrate-degrading enzyme but renders the coordination site accessible to intracellular water in the presence of the carbohydrate-degrading enzyme.

31. The method of claim 30, wherein the carbohydrate is selected from the group consisting of galactose, glycogen, or glucose.

32. The method of claim 18, wherein the opaque medium comprises brain cells or brain tissue in vivo, wherein said introducing comprising administering the contrast agent to a human or non-human subject intravenously or intravascularly.

33. The method of any of claims 18 to 32, wherein said visualizing is done grossly with the naked eye or using microscopy.

34. The method of any of claims 18 to 33, wherein said visualizing is carried out by one or more modalities selected from the group consisting of fluorescence imaging, magnetic resonance imaging (MRI), and computer-aided tomography (CAT).

35. The method of any of claims 18 to 34, wherein said visualizing is carried out by two or more modalities selected from the group consisting of fluorescence imaging, magnetic resonance imaging (MRI), and computer-aided tomography (CAT), and wherein said visualizing is carried out simultaneously or consecutively.

36. The method of claim 18, wherein the target comprises a stem cell or progenitor cell *in vitro* or *in vivo*.

37. The method of claim 18, wherein the target comprises a differentiated cell *in vitro* or *in vivo*.

38. The method of claim 18, wherein the quantum dot further comprises a Dys/SiO₂ Dys/SiO₂ coating (outer shell), and wherein said visualizing comprises carrying out magnetic resonance imaging (MRI).

39. The method of claim 18, wherein the quantum dot further comprises a Dys/SiO₂ Dys/SiO₂ coating (outer shell), and wherein said visualizing comprises carrying out magnetic resonance imaging (MRI) using a magnetic field above 4 Tesla.

40. The method of claim 18, wherein the target comprises a genetically modified cell *in vitro* or *in vivo*.

41. A mammal cell containing a multi-functional contrast agent of any of claims 1 to 17.

42. The mammal cell of claim 41, wherein said cell is isolated.

43. The mammal cell of claim 41, wherein said cell is a human cell.

44. The mammal cell of claim 41, wherein said cell is a stem cell or progenitor cell.

45. The mammal cell of claim 41, wherein the cell is a differentiated cell.

46. The mammal cell of claim 41, wherein said cell is a cancer cell.

47. The mammal cell of claim 41, wherein said cell is a tumor cell.

48. The mammal cell of claim 41, wherein said cell is a genetically modified cell.

49. The mammal cell of claim 41, wherein said cell is a primary cell.

50. The mammal cell of claim 41, wherein said cell is a cell of a cell line.